Amendments to the Specification

On page 1, at lines 10-17, please amend the specification as follows.

This application is a National Phase application of PCT/US01/18611 filed on June 8, 2001, published in English, which claims priority from United States patent application 09/591,642, filed June 9, 2000, and is a continuation of United States patent application 09/591,642, filed June 9, 2000, which is a continuation-in-part of U.S. patent application 09/244,340 to Toh et al., filed February 4, 1999 and U.S. patent application 09/372,954 to Toh et al., filed August 12, 1999, now issued U.S. Patent No. 6,429, 017, the subject matter of each being incorporated herein by reference. This application also relates to U.S. patent 5,646,046 to Fischer et al., the subject matter of which is incorporated herein by reference.

The following list of claims will replace all prior versions and listings of claims in the application.

1. (Currently Amended) A method of diagnosing hemostatic dysfunction comprising an inflammatory condition, said method comprising:

a) adding one or more reagents to a test sample from a patient comprising at least part of a blood sample from the patient in order to cause formation of a complex comprising at least C-Reactive protein and at least one human lipoprotein, while causing substantially no fibrin polymerization, wherein the one or more reagents comprises a divalent metal ion;

b) measuring the formation of said complex over time so as to derive a time-dependent measurement profile; ~~and~~

c) determining a slope and/or total change in the time-dependent measurement profile so as to diagnose hemostatic dysfunction in the patient; and

d) correlating the increase in steepness of the slope with an increase likelihood of mortality associated with hemostatic dysfunction in the patient.

2. (Canceled)

3. (Previously Presented) The method according to claim 1, wherein said metal ion is a divalent metal ion selected from the group consisting of one or more of calcium, magnesium, manganese, iron or barium.

4. (Previously Presented) The method according to claim 3, wherein said divalent metal ion is calcium.

5. (Previously Presented) The method according to claim 1, wherein said reagent comprises calcium chloride.

6. (Original) The method according to claim 1, wherein a clot inhibitor is provided as part of said reagent or as part of an additional reagent added to said test sample.

7. (Original) The method according to claim 6, wherein said clot inhibitor comprises one or more of hirudin, heparin, PPACK, I2581, and antithrombin.

8. (Original) The method according to claim 1, wherein the formation of said complex is correlated to the increase probability of death of the patient.

9. (Original) The method according to claim 8, wherein the greater the formation of said complex, the greater the likelihood of death of the patient.

10. (Original) The method according to claim 1, wherein the time dependent measurement profile is an optical transmission profile, and wherein the greater the decrease of optical transmittance through the test sample, the greater the formation of said complex, and the greater the likelihood of mortality of the patient.

11. (Previously Presented) The method according to claim 1, wherein said at least one human lipoprotein comprises one or more of chylomicrons or remnants thereof, VLDL, IDL, LDL or HDL.

12. (Previously Presented) The method according to claim 11, wherein diagnosing hemostatic dysfunction in the patient comprises a prediction of the likelihood of mortality of the patient.

13. (Previously Presented) The method according to claim 1, wherein said one or more reagents is added to said test sample in the absence of clot inducing reagents.

14. (Previously Presented) The method according to claim 1, wherein the formation of a precipitate is measured at least once after time zero.

15. (Previously Presented) The method according to claim 14, wherein a single endpoint measurement is made of precipitate formation after time zero.

16. (Previously Presented) The method according to claim 1, wherein said one or more reagents is capable of causing precipitate formation completely in the absence of fibrin polymerization.

17. (Previously Presented) The method according to claim 10, wherein the amount of fibrin polymerization, if any, causes no change in optical transmittance.

18. (Previously Presented) A method for predicting an increased likelihood of system failure or mortality of a patient, comprising:

a) obtaining a blood sample from a patient;

b) obtaining plasma or serum from said blood sample;

c) adding one or more reagents capable of inducing the formation of a protein complex comprising at least one lipoprotein and at least one acute phase protein wherein the one or more reagents comprise a metal ion;

d) taking one or more measurements of a parameter of the plasma or serum and correlating the measured parameter to complex formation if present; and

e) correlating the formation of the complex to an increased likelihood of

system failure or mortality of the patient.

19. (Original) The method according to claim 18, wherein a plurality of measurements are made after addition of said one or more reagents in order to derive a time-dependent measurement profile.

20. (Original) The method according to claim 18, wherein a single reagent is used prior to taking said measurements.

21. (Original) The method according to claim 18, wherein said measurements are measurements of optical transmission or absorbance through said sample.

22. (Canceled)

23. (Previously Presented) The method according to claim 18, wherein said metal ion comprises one or more of calcium, magnesium, manganese, iron or barium.

24. (Original) The method according to claim 18, wherein a clot inhibitor is provided as part of said one or more reagents.

25. (Original) The method according to claim 24, wherein said clot inhibitor comprises one or more of hirudin, heparin, PPACK, I2581 or antithrombin.

26. (Original) The method according to claim 18, wherein said one or more measurements are unaffected by clot formation due to lack of fibrin polymerization.

27. (Previously Presented) The method according to claim 18, wherein the one or more measurements are a plurality of measurements, and wherein a rate of change of said plurality of measurements or a total change is determined, and wherein hemostatic dysfunction is determined based on the determined total and/or rate of change.

28. (Original) The method according to claim 18, wherein said at least one lipoprotein comprises VLDL, IDL and/or LDL, and said at least one acute phase protein comprises SAA and/or CRP.

29. (Original) The method according to claim 28, wherein a majority of said complex comprises CRP bound to VLDL.

30. (Original) The method according to claim 18, wherein the prediction of the increased likelihood of system failure or mortality is more accurate than in the absence of steps a) to e).

31. (Original) The method according to claim 18, wherein steps a) to e) are performed at least once more at a later time in order to determine patient condition regression or progression.

32. (Previously Presented) A method for diagnosis or monitoring of a hemostatic dysfunction comprising an inflammatory condition, said method comprising a confirmatory assay of determining the extent of inhibition of precipitation by a precipitate inhibiting reagent comprising:

a) adding one or more reagents to a test sample comprising at least a component of a blood sample from a patient in order to cause formation of a precipitate comprising an acute phase protein and a lipoprotein, wherein the one or more reagents comprises a metal ion;

b) measuring the precipitate comprising the acute phase protein and the lipoprotein;

c) adding a precipitate inhibiting reagent, before or after adding said one or more precipitate causing reagents, which inhibits at least in part the formation of the precipitate; and

d) determining the extent of inhibition of precipitation by said precipitate inhibiting reagent.

33. (Original) The method of claim 32, wherein said precipitate inhibiting reagent is added after all or substantially all of the lipoprotein has become associated with acute phase protein so as to form said precipitate.

34. (Original) The method of claim 32, wherein said precipitate inhibiting reagent is added prior to adding the precipitate causing reagent.

35. (Previously Presented) The method of claim 32, wherein said precipitate causing reagent is a divalent metal cation.

36. (Previously Presented) The method of claim 32, wherein said precipitate inhibiting reagent comprises one or more of an apolipoprotein capable of binding to CRP, a phosphorylcholine, sphingomyelin, EDTA, sodium citrate, or an antibody capable of specifically binding to a lipoprotein-acute phase protein binding site.

37. (Original) The method of claim 36, wherein said precipitate inhibiting reagent is capable of inhibiting the association of CRP with chylomicrons or remnants thereof, LDL, VLDL and/or IDL.

38. (Original) The method of claim 37, wherein the determining of the extent of inhibition is performed over time so as to derive a time-dependent measurement profile.

39. (Original) The method of claim 38, wherein the measurement over time is a measurement of optical transmittance or absorbance over time.

40. (Previously Presented) A method for diagnosis or monitoring of a hemostatic dysfunction comprising an inflammatory condition, said method comprising correlating the formation of a complex to a concentration of one or more lipoproteins comprising:

a) providing a test sample from a test subject;

b) adding one or more reagents to said test sample in order to cause formation of a complex of one or more lipoproteins and one or more acute phase proteins, wherein said reagent comprises a divalent metal cation and an acute phase protein;

c) measuring the formation of the complex; and

d) correlating the formation of the complex to a concentration of said one or more lipoproteins observed in patients with said hemostatic dysfunction, wherein the formation of an initial complex and the formation of an additional complex are measured over time so as to provide respective first and second time-dependent measurement profiles.

41. (Canceled)

42. (Previously Presented) The method of claim 40, wherein said acute phase protein is CRP.

43. (Previously Presented) The method of claim 40, wherein said one or more lipoproteins is chylomicrons, VLDL and/or IDL.

44. (Canceled)

45. (Original) The method of claim 40, wherein the measured additional complex and the measured initial complex together are correlated to a total amount of acute phase protein in the test sample.

46. (Original) The method of claim 44, wherein the acute phase protein is C-reactive protein.

47. (Original) The method of claim 40, wherein the measured initial complex is correlated to a likelihood of system failure and/or mortality.

48. (Previously Presented) The method of claim 47, wherein the greater the initial complex measured, the greater the likelihood of system failure and/or mortality.

49. (Previously Presented) A method for testing the effectiveness of a therapeutic for treatment of hemostatic dysfunction, comprising:

a) providing from a test subject a test sample to be tested for complex formation;

b) adding one or more reagents which causes formation of a complex of acute phase protein and lipoprotein present in said test sample, wherein the reagent comprises a metal ion;

c) administering to said test subject a therapeutic suspected of being useful in the treatment of hemostatic dysfunction;

d) repeating steps a) and b); and

e) determining if the amount of complex formed has changed.

50. (Currently Amended) A method of diagnosing hemostatic dysfunction comprising:

a) adding ~~calcium~~ a metal divalent ion and one or more clot inhibitors to a blood sample from a patient in order to cause formation of a complex comprising C reactive protein (CRP) and at least one human lipoprotein selected from the group consisting of very low density lipoprotein (VLDL) and intermediate density lipoprotein (IDL), while causing substantially no fibrin polymerization;

b) measuring the formation of said complex over time so as to derive a time-dependent measurement profile; and

c) determining a slope and/or total change in the time-dependent measurement profile; and

d) correlating the formation of the precipitate to the likelihood of mortality, the greater the formation of said complex, the greater the likelihood of death of the patient.

51. (Previously Presented) The method of claim 50, wherein the hemostatic dysfunction is disseminated intravascular coagulation (DIC).

52. (Currently Amended) A method for testing the effectiveness of a therapeutic for treatment of hemostatic dysfunction, comprising *(a)*monitoring the formation of a complex comprising C reactive protein (CRP) and at least one human lipoprotein selected from the group consisting of very low density lipoprotein (VLDL) and intermediate density lipoprotein (IDL), and *(b)* correlating the decrease of complex formation with effectiveness of a therapeutic for treatment of hemostatic dysfunction.

53. (Previously Presented) The method of claim 52, wherein the hemostatic dysfunction is disseminated intravascular coagulation (DIC).

54. (Currently Amended) A method of diagnosing hemostatic dysfunction comprising an inflammatory condition, said method comprising:

a) adding calcium to a blood sample from a patient in order to cause formation of a complex comprising at least C-Reactive protein and at least one human lipoprotein, while causing substantially no fibrin polymerization;

b) measuring the formation of said complex over time so as to derive a time-dependent measurement profile; and

c) determining a slope and/or total change in the time-dependent measurement profile; and

d) correlating the formation of the precipitate to the likelihood of mortality, the greater the formation of said complex, the greater the likelihood of death of the patient.

55. (New) The method of claim 50, wherein the metal divalent ion is calcium.